REMARKS

Applicants again want to thank the Examiner for the courtesy of conducting a telephone interview with applicants' representative.

Claims 1-14 are in this application. It is claims 1, 12, 13 and 14 have been amended. Claim 1 has been amended to include a description of Aib, Deg, Dpg, and Ac5c. Support for this amendment is found on page 4 of the specification.

Claim 13 has been amended to define the cancer as breast, colon, lung, pancreatic, oral, ovarian, stomach, prostate, laryngeal and duodenum and glioblastoma and leukemia. Support for this is found on pages 15-21 of the specification.

It is respectfully requested that claims 21-51 be entered into this application. Claims 21-51 are claims for compositions of the peptides of claims 2-12 and method claims for the treatment of cancer using peptides of claims 2-12.

The Examiner has rejected claims 1-14 under 35 USC 112, first paragraph as not being enabled. Applicants respectfully traverse this rejection.

Applicants disagree with the Examiner's contention that the claims are not enabled for treatment of all types of cancer.

Firstly, it is incorrect to include claims 1-12 in this rejection. Claims 1-11 define peptides and as noted by the Examiner at the bottom of page 3 of the Office Action, the specification is enabling for the peptides.

There is a description of the peptides, how to make them and how to use them in this application.

This is clearly sufficient to teach one skilled in the art how to make and use the invention of claims 1-14.

Applicants also respectfully disagree with the Examiner's rejection of claims 13 and 14. It is well known to screen candidates for anticancer effect in *in vitro* systems and *in vivo* animal models. Testing of anticancer compounds is standard in the art to identify cytotoxic compounds.

It is a common and standard practice and norm for testing molecules for anticancer activity in vitro on human tumor cell lines. (Br J Cancer. 2001 May 18; 84(10):1289-90 (Flasks, Fibres and Flanks - Preclinical tumor models for predicting clinical antitumor activity). The authors report that in vitro activity against 6 or more lung or breast cancer cell lines does predict xenograft activty against these tumor types. In articles "Semin Oncol 1992 Dec.; 19(6):622-38 (The National Cancer Institute: cancer drug discovery and development program) and "Jpn J Antibiot 1977 Dec.;30 Suppl:35-40 (Antitumor screening procedures of the National Cancer Institute)" extensive use of human tumor cell lines for identification of potential cytotoxic drugs is described.

Examples 12, 13 and 14 describe the use of the compounds of this invention *in vitro* assays. Attached is a declaration by Dr. Rama Mukherjee in which she decribes that a peptide of SEQ ID NO:11 inhibited the growth of colon adenocarcinoma *in vivo* by 53%.

Therefore, based on the data in this application, the relationship between cytotoxic effects shown *in vitro* and *in vivo,* the declaration of Dr. Mukherjee and the reasons set out in the previous response, claims 13 and 14 are enabled.

However, to expedite prosecution claim 13 has been amended to define the cancer that is treated to breast, colon, lung, pancreatic, oral, ovarian, duodenum, laryngeal, stomach, or prostate, or glioblastoma or leukemia. As explained above, the use of the compounds of this invention to treat these types of cancers is supported in examples 12-14 and by the results set out in Dr. Mukherjee's declaration.

Based on this and the knowledge of one skilled in art, one skilled in the art would be able to treat cancer and specifically the cancers included in claim 13 using an effective amount of a peptide of claim 1. During the interview the Examiner indicated that she would consider method claims that are limited to specific types of cancer favorably.

Therefore, it is respectfully requested that this rejection be withdrawn.

Applicants preserve all rights to file one or more divisional applications directed to subject matter disclosed and not currently claimed in this application.

The Examiner has rejected claims 1-14 under 35 USC 112, second paragraph as being indefinite. Applicants respectfully traverse this rejection.

As discussed with the Examiner during the interview, there is no requirement that the function or activity of the peptides be included in claim 1 . The Examiner was requested to provide a legal basis for this rejection and the Examiner has not provided one. According to MPEP 2173.05(g) a functional limitation is an attempt to define something by what it does, rather than by what it is. Claim 1 can be defined by its chemical structure and there is no requirement to include a function or activity in a claim to a chemical compound.

The Examiner also states that the use of the term an effective amount is indefinite. Applicants respectfully disagree. The term an effective amount is a term used in the art and is defined on page 8, lines 22-24. In addition, the application contains information on the amount of the peptides that can be used to kill tumor cells.

Chemotherapeutic is a term well known in the art. Attached is a definition from the American Heritage Dictionary for the English language.

Therefore, it is respectfully requested that this rejection be withdrawn.

Applicants submit that the present application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,

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IN THE CLAIMS

Please amend the following claims:

1. (Amended) A peptide of the formula

X-D-Phe-Gln-R1-R2-Val-R3-His-R4-NH_2

wherein X is acetyl or straight, branched or cyclic alkanoyl group from 3-16 carbon atoms, or X is deleted

R1 is Trp or D-Trp,

R2 is Ala, Aib or Deg,

R3 is Gly, Aib, Deg, Dpg or Ac5c,

R4 is Leu or Ile

or a hydrolyzable carboxy protecting group; wherein at least one of R2 or R3 is an α,α-dialkylated amino acid; or a pharmaceutically acceptable salt of the peptide wherein Aib is α-aminoisobutyric acid, Deg is α,α-diethyl glycine, Dpg is α,α-di-n-propyl glycine and Ac5c is 1-amino-cyclo pentane carboxylic acid.

12. (Amended) A composition comprising an effective amount of a [polypeptide] peptide according to claim 1, and a pharmaceutically acceptable carrier.

13. (Amended) A method of treatment of cancer in mammals which comprises [the administration] administering of an effective amount of a peptide according to claim 1 wherein the cancer is colon, lung, prostate, stomach, laryngeal, oral, breast, duodenum, ovarian or pancreatic or leukemia or glioblastoma.

14. (Amended) A method according to claim [11] 13, further comprising administering a chemotherapeutic compound.

DECLARATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of : 09/630,333 Serial No:

Filed: July 31, 2000 Examiner:

For:

Attorney docket:

Assistant Commissioner for Patents
Washington, D.C. 20231

I, Rama Mukherjee, M.Sc., Ph.D., FNASc, Director, Dabur Research Foundation, a citizen of India with major contribution in the field of cancer therapeutics, neurobiology, and mycobacterial immunology, and having filed more than 30 patent applications and with over hundred publications in international and national journals declare that I have read and understood the specification of US patent application.

The following experiment was conducted.

Example

Pharmaceutical composition and method of administration to a patient for treatment of cancer

The invention provides a method for treating a mammal (including a human being) afflicted with cancer. The types of cancer that may be treated include, but are not necessarily limited to, cancers of breast, pancreas, stomach, oral, lung, colon, ovary leukemia, prostate, glioblastoma, and larynx .

The method of this invention comprise, consist of, or consist essentially of

administering systemically to the mammal a therapeutically effective dose of peptide SEQ ID : 3, SEQ ID : 4, SEQ ID : 5, SEQ ID : 6, SEQ ID : 7 SEQ ID : 8, SEQ ID : 9, SEQ ID : 10, SEQ ID : 11, SEQ ID : 12 or SEQ ID : 13. The dose of the peptide ranges between 0.25 μg /Kg. BWt to 500 μg /Kg. BWt, and more preferably in the range of 10 μg /Kg. BWt to 200 μg /Kg. BWt. However, the dose dependent on the effects sought, the manner of administration, the peptide selected, and the cancer being treated. Systemic administration refers to oral, rectal, nasal, transdermal, and parentral (i.e., intramuscular, intravenous, and subcutaneous). In accordance with good clinical practice, it is preferred to administer the composition at a dose that will produce anticancer effects without causing undue harmful side effects. The composition may be administered either alone or as a mixture with other therapeutic agents.

The composition may optionally and preferably contain pharmaceutically acceptable diluents, excipients, solvents, binders, stabilizers, and the like. Such diluents may include: RPMI 1640, buffered saline, isotonic NaCl, Ringer's solution, water, distilled water, polyethylene glycol (neat or in water), 2% tween in water, dimethylsulfoxide to 50% in water, propylene glycol (neat or in water), phosphate buffered saline, balanced salt solution, glycerol, and other conventional fluids that are suitable for intravenous administration. Pharmaceutical compositions, which provide from about 0.1 to 10.0 mg of the composition per unit dose are preferred and are conventionally prepared as tablets, lozenges, capsules, powders, aqueous or oily suspensions, syrups, elixirs, and aqueous solutions. The nature of the pharmaceutical composition employed will, of course, depend on the desired route of administration

Protocol and method of treating an animal with cancer using SEQ ID : 11

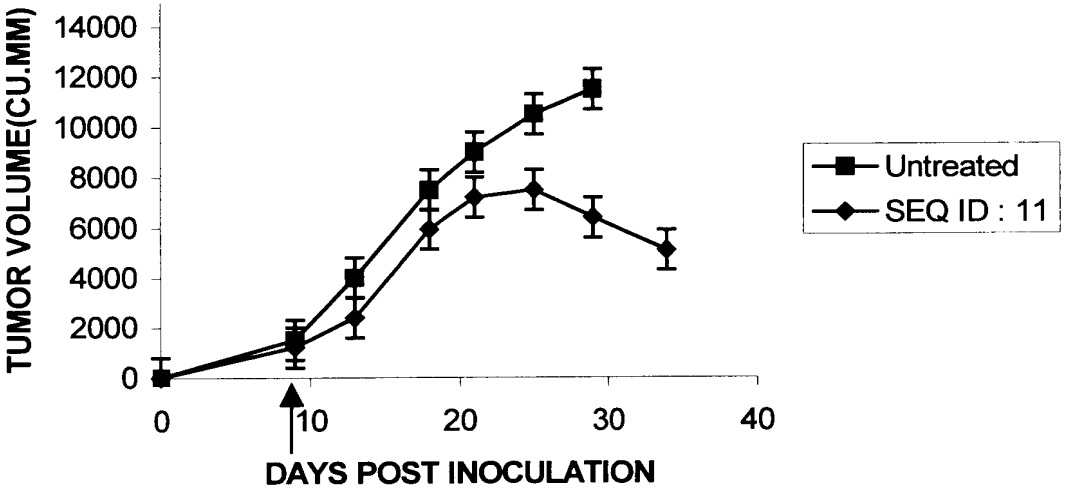
Primary tumor cells of colon adenocarcinoma (PTC) xenografts were initiated in Balb/c athymic mice by subcutaneous inoculation of a single cell suspension of PTC cells(15×10^6 cells/100 μL). When the average tumor volumes, as measured using a vernier caliper, were between 400 – 800 mm^3 treatment was initiated on the tumor

bearing animals which were divided into two groups of three animals each including one untreated control group. SEQ ID : 11 was prepared at a concentration of 42.5 μg/ml by solubilizing the said amount of peptide in water. The solubilized peptide was administered intravenously at a dose of 4.25 μg/100 μL twice a day. The antitumor activity was monitored by measuring tumor volumes every fourth day using the formula W*W*L*0.4 (W = smaller dia, L = larger dia). It may be noted that all control (untreated) animals died by day 29 post treatment. The percentage inhibition of tumor growth was calculated using the formula (1- tumor volume(treated) / tumor volume (control))* 100.

The results are:

Adjoining figure shows the pattern of tumor growth till day 34 in treated and day 29 in untreated animals. The percentage inhibition of tumor growth caused by SEQ ID : 11 as compared to untreated on day 29 was 53%.

INVIVO ANTITUMOR EFFECT OF SEQ ID : 11(Dose x = 8.5 ug/day) ON PTC XENOGRAFTS



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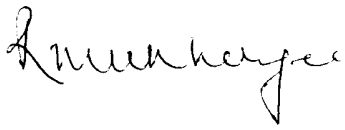
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statement may jeopardize the validity of the application or any patent issued thereon.

Signed this14th day of February 2003.

Signature



che mo ther a py

(click to hear the word) (kē'mō-thĕr'ə-pē, kĕm'ō-)
n.

1. The treatment of cancer using specific chemical agents or drugs that are selectively destructive to malignant cells and tissues.
2. The treatment of disease using chemical agents or drugs that are selectively toxic to the causative agent of the disease, such as a virus, bacterium, or other microorganism.

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che'mo ther'a peu'tic
(-pyo͞o'tĭk) ***adj.***
che'mo ther'a peu'ti cal ly ***adv.***
che'mo ther'a pist ***n.***
